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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/626,219	07/26/2000	Jeffrey Browning	A046 US	7978

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LAHIVE & COCKFIELD, LLP.  
28 STATE STREET  
BOSTON, MA 02109

EXAMINER
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YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 12/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/626,219

Applicant(s)

BROWNING ET AL.

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 11 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 20,24-26,31-33 and 36-51 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 20,24-26,31-33 and 36-51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09-11-2003 has been entered.

Claims 20, 26, 31, 32, have been amended and claims 36-51 have been newly added. Claims 20, 24-26, 31-33, and 36-51 are pending and under consideration.

### *Claim Rejections - 35 USC § 112*

The rejection of claims under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **withdrawn** because applicant's argument is persuasive.

Claims 20, 24-26, and 31-33 **remain rejected**, and the new claims 36-51 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are interpreted as drawn to method of treating follicular lymphoma by administering composition comprising a soluble lymphotoxin beta receptor to a subject (base claims

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20 and 43), to a mammal (claim 24) or to a human (claims 25), wherein the dependent claims 26, 36, 44, and 45 describe what happen after said administering said composition, wherein dependent claims 31-33 further comprises another known cancer therapy, wherein claims 37-42, and 46-51 further limits what other things could be attached to said soluble lymphotoxin beta receptor.

Applicant argues that the instant specification describes cancer treatment method using an art-accepted lymphoma animal model, namely SJL/RCS mice; weight determination is an art-accepted way of checking whether a certain compound works as anti-tumor agent as shown in Exhibits A-D (peer-reviewed journal articles); administering the soluble lymphotoxin beta receptor fused to human IgG Fc indeed results in lower lymph node (LN) weight in SJL/RCS mice. These arguments have been fully considered but found unpersuasive for following reasons.

The Office considered the data presented in the instant specification as well as what is known about the activity of a soluble lymphotoxin beta receptor in the art including applicant's numerous US patents and WIPO documents as well as other peer-reviewed journal articles.

The Office cite US Patent 5, 925, 351, Higuchi et al (Biochem Biophys Res Commun. 1992 Jan 31;182(2):638-43), Qin et al ( 1995, Blood, vol. 85, 2779-85), Wong et al (1996, Journal of Cellular Biochemistry, vol. 6-, pages 56-60), and Reisfeld et al (April 15, 1996, Cancer Res. Vol. 56, pages 1707-12) in order to demonstrate the state of art regarding the biological activity of a soluble lymphotoxin beta receptor in analysis

of why one skilled in the art would have questioned the efficacy of a soluble lymphotoxin beta receptor in treatment of lymphoma.

US Patent 5, 925, 351 (one inventor common with the instant application) at Figure 2 (note the Figure legend at column 4 lines 63-65) teaches that a soluble lymphotoxin beta receptor inhibits LT-induced cell death. Also note the abstract teaches a soluble lymphotoxin beta receptor binds to its ligand, lymphotoxin, thereby blocking LT signaling.

Higuchi et al (note Fig. 4 at page 641) teach a soluble receptor to lymphotoxin has the exactly the opposite effect of what the instant claims say i.e., preventing the anti-proliferative effect of the ligand; this result is in agreement with the teaching of US Patent 5, 925, 351 above.

Either Qin et al (note Fig. 2, for example), Reisfeld et al (note Tables 1 and 2, for example) teach that lymphotoxin has anti-tumor effect. By administering a soluble receptor lead to suppression of the LT signaling as taught by either US Patent 5, 925, 351 or Higuchi et al, thus leading to suppression of apoptosis. Note Fig. 4 of Wong et al (1996, Journal of Cellular Biochemistry, vol. 6-, pages 56-60) for pictorial explanation, showing that the ligand binding to the receptor signals cell to die.

Thus, art as a whole teaches that a soluble lymphotoxin beta receptor **inhibits** LT signaling system, which will lead to more cell proliferation, not death. As for the lower LN weight observed for SJL/RCS mice who received the soluble lymphotoxin beta receptor, one in the art might look for explanation elsewhere because Ponzio et al (IDS, 1986, Intern. Rev. Immunol., vol. 1, pages 273-301) at page 288-291 teach unlike other

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tumor growth, immunosuppression have an adverse effect to transplantability of RCS. US Patent 5, 925, 351 teaches a soluble lymphotoxin beta receptor results in immunosuppression. See Fig. 5 along with the claims. Based on Ponzio et al and the US patent, one would conclude that SJL/RCS mice who received the soluble lymphotoxin beta receptor did not have RCS not fully transplanted, thus lower LN weight, which is different than lower LN weight due to reducing of tumor volume of fully transplanted tumor.

Thus, one skilled in the art would have questioned the efficacy of a soluble lymphotoxin beta receptor in treatment of lymphoma since the art as a whole teaches a soluble lymphotoxin beta receptor would make tumor cells grow better rather than killing said cells.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*pc 12/15/13*  
Misook Yu  
December 13, 2013

  
ANTHONY G. CARLINI  
EXTERNSORY PATENT ATTORNEY  
TECHNOLOGY, INC.